REMARKS

Claims 1-10 and 12-13 are pending in the present application. With this Amendment, Claims 1 and 2 are being amended. No claims are being added. The amendments and the rejections raised in the Office Action are discussed in detail below.

Claim Amendments

Claims 1 and 2 have been amended. Support for amended Claim 1 is found in the specification at page 10, lines 12-13, and page 11, lines 17-19. Claim 2 was amended to correct antecedent basis. No new matter is added by the amendments. Accordingly, entry into the instant Application is proper and respectfully requested.

Claim Rejections under 35 U.S.C. §102(e)(1)

Glimcher *et al.* US Patent No. 5,958,671

Claims 1-4 and 6-9 are rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Glimcher *et al.* (US Patent No. 5,958,671). To anticipate a claim, the reference must teach every element of the claim. M.P.E.P §2131. *Glimcher* does not anticipate Claims 1-4 and 6-9.

Amended Claim 1, the only independent claim, recites a method for screening for an agent which modulates transcription factor activity, comprising providing a cell comprising a transcription factor of interest and a vector comprising a binding site for said transcription factor of interest operatively linked to a reporter gene, introducing a plurality of candidate agents comprising a pool of expression vectors, each comprising transcriptional and translational regulatory nucleic acid operably linked to nucleic acid encoding a polypeptide, and determining the activity of said transcription factor by measuring the expression of said reporter gene, wherein a change in activity between the presence and absence of said candidate agents indicates the presence of an agent which modulates transcription factor activity.

The Examiner asserts *Glimcher* teaches methods for screening for a plurality of compounds that modulate the expression and/or activity of the transcription factor in a cell. Office Action at page 3. The Examiner points to, *inter alia*, column 4, lines 15-31, for support for the assertion. *Glimcher* is directed to the study of methods of modulating production of Th2-associated cytokines by modulating the activity of a transcription factor, c-Maf. One aspect disclosed by *Glimcher*

involves screening assays for identifying a compound that modulates the activity of a transcription factor that regulates expression of a Th2-associated cytokine gene. Importantly, the sections of *Glimcher* that the Examiner cites for support are in fact directed to the screening of individual compounds that modulate individual proteins. For example,

> [t]he methods of the invention can further involve the use of **additional agents** that modulate the activity of **additional transcription factors** that contribute to regulating the expression of Th1- or Th2-associated cytokines. Preferred additional agents are those which modulate the activity of a Nuclear Factor of Activated T cells (NF-AT) protein. Thus, in one embodiment, a stimulatory method of the invention can involve the use of a **first agent** that stimulates the expression and/or activity of a **maf protein** and a **second agent** that stimulates the expression and/or activity of an **NF-AT protein**. ... Alternatively or additionally, the modulatory methods of the invention can involve the use of **additional agents** that modulate the activity of an **AP-1 family protein**. Glimcher at column 4, lines 8-24 (emphasis added).

Thus, *Glimcher* does not teach the introduction of a plurality of candidate agents comprising a pool of expression vectors, each comprising an expression regulatory nucleic acid operably linked to nucleic acids encoding a polypeptide, and determining the activity of said transcription factor by measuring the expression of said reporter gene, as required by Claim 1. Because *Glimcher* does not teach every element of Claim 1, it cannot anticipate Claim 1, or Claims 2-4 and 6-9 dependent thereon. Applicants respectfully request withdrawal of the rejection.

Additionally, the Examiner asserts that *Glimcher* anticipates Claim 2, by teaching the agent that modulates transcription factor activity can be a cDNA clone from an expression library. The Examiner points to, *inter alia*, column 3 lines 53-57, and column 8, lines 61-66, as support for the assertion. Applicants respectfully submit that *Glimcher* does not teach introducing a cDNA expression library. For example, *Glimcher* at column 3 lines 53-57, discloses antisense nucleic acids molecules that are complementary to a Maf family gene, but makes no mention of introducing a cDNA expression library. *Glimcher* at column 8 lines, lines 61-66 discloses the expression of a Maf family protein in a cell with a vector encoding Maf cDNA, but makes no mention of introducing a cDNA expression library.

Furthermore, the Examiner asserts that *Glimcher* anticipates Claim 3 because *Glimcher* teaches introducing into the indicator cell a control plasmid comprising a constitutively expressed gene to monitor transfection efficiency. The Examiner cites to column 5, lines 29-61 and Figures 3-4 for support for the assertion. Applicants respectfully submit that *Glimcher* does not teach the use a control plasmid comprising a constitutively expressed gene to monitor transfection efficiency. Rather, *Glimcher*, at column 38 lines 4-6, describes Figure 3 as cotransfection experiments demonstrating that expression of c-Maf in the Th1 clone AE7 results in activity of the IL-4 promoter reporter after stimulation through the T cell receptor, but makes no mention of the use of a second plasmid to monitor transfection efficiency. Likewise Figure 4, and column 5 lines 50-60, makes no mention of the use of a second plasmid to monitor transfection efficiency. As such, *Glimcher* does not teach the use of a control plasmid comprising a constitutively expressed gene to monitor transfection efficiency and cannot anticipate Claim 3.

Applicants respectfully request withdrawal of the rejections.

Kushner *et al.* WO 99/11760

Claims 1 and 3-9 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Kushner *et al.* (WO 99/11760). *Kushner* does not anticipate Claims 1 and 3-9.

Claim 1 recites a method for screening for an agent which modulates transcription factor activity as described above.

Kushner is directed to the study of methods for screening nuclear transcription factor ligands for the ability to modulate estrogen activation at an AP-1 site. The Examiner states that *Kushner* teaches that "any compounds can be screened according to their invention, especially those with antiestrogenic activity". Office Action at page 5. However, the disclosure of "any compound" is merely an invitation to experiment and that there is no specific disclosure or suggestion to use a pool of expression vectors as set forth in Claim 1. As such *Kushner* fails anticipate Claim 1 or Claims 3-9 dependent thereon.

Furthermore, the Examiner asserts that *Kushner* anticipates Claim 3 because *Kushner* teaches introducing into the indicator cell a control plasmid comprising a constitutively expressed gene to monitor transfection efficiency. The Examiner cites to page 33-34 and Figures 2-4 for support for the assertion. However, *Kushner*, at page 33, lines 10-12, teaches cotransfection of cells with an estrogen receptor expression plasmid and a reporter plasmid containing a lucerferase gene under the

transcriptional control of an estrogen response element. As such, *Kushner* does not teach the use of a control plasmid comprising a constitutively expressed gene to monitor transfection efficiency.

Applicants respectfully request withdrawal of the rejection.

Cen *et al.* US Patent Application No. 2003/0170656

Claims 1-2 and 4-10 and 12-13 are rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Cen *et al.* (US Patent Application No. 2003/0170656). To anticipate a claim, the reference must teach every element of the claim. M.P.E.P §2131. Applicants respectfully submit that *Cen* does not do so.

Claim 1 recites a method for screening for an agent which modulates transcription factor activity as described above.

The Examiner asserts the *Cen* teaches (i) providing a cell comprising a transcription factor of interest and a vector comprising a binding site for the transcription factor of interest operatively linked to a reporter gene and (ii) introducing a plurality of candidate agents to the cell. Office Action at pages 5-6. The Examiner points to, *inter alia*, paragraphs 4 and 61 for support for the assertion. *Cen* teaches that when a transcription factor that acts at a regulatory sequence is "sought", the regulatory sequence is linked to a reporter gene. *Cen* at paragraph 61. With regard to such a construction, *Cen* teaches a method for screening for transcriptional factors that result in the expression of the reporter gene. *Cen* does not teach the use of a vector comprising a pool of expression vectors as candidate agents, as required by Claim 1. Because *Cen* does not teach every element of Claim 1, it cannot anticipate Claim 1, or Claims 2, 4-10 and 12-13 dependent thereon. Applicants respectfully request withdrawal of the rejections.

Claim Rejection under 35 U.S.C. §103

Cen *et al.* in view of Kushner *et al.*

Claim 3 is rejected under 35 U.S.C. §103 as allegedly being obvious over Cen *et al.* (US Patent App. No. 2003/0170656) in view of Kushner *et al.* (US Pub. No. US2002/0098477). The rejection is traversed on the grounds that the Patent Office has failed to establish a *prima facie* case of obviousness.

Section 103(a) precludes the grant of a patent only if "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains." 35 U.S.C. § 103(c). The Patent Office bears the initial burden of establishing a case of *prima facie* obviousness. *In re Bell*, 26 USPQ2d 1529, 1530 (Fed. Cir. 1993); *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1998); MPEP § 2142. If the Patent Office does not establish a *prima facie* case, the Applicant is under no obligation to submit evidence of nonobviousness, and the rejection must be withdrawn. *Id.*

There are three requirements to establish a *prima facie* case of obviousness: 1) there must be some suggestion or motivation, either in the references or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine the reference teachings; 2) there must be a reasonable expectation of success; and 3) the prior art reference must teach or suggest all the claim limitations. M.P.E.P §2143.

The Examiner asserts that *Cen* fails to teach introducing control plasmid comprising a constitutively expressed gene to monitor transfection efficiency into a cell and that the teachings in *Kushner* supplement *Cen's* deficiencies. Office Action at page 8.

Claim 3 is dependent on Claim 1 as discussed above. Thus Claim 3 recites a method for screening for an agent as set forth in Claim 1 and further comprising introducing into said cell a control plasmid comprising a constitutively expressed gene to monitor transfection efficiency.

As set forth in the section above discussing anticipation, *Cen* fails to teach a method for screening for an agent, as set forth by Claim 1. Thus, *Cen* and *Kushner* taken together fail to teach or suggest all of the elements of independent Claim 1. Therefore, Claim 3 is not obvious in view these references. Applicants request withdrawal of this rejection.

Cen *et al.* in view of Kushner *et al.*

Claim 5 is rejected under 35 U.S.C. §103 as allegedly being obvious over Glimcher *et al.* (US Patent No. 5,958,671) in view of Kushner *et al.* (US Pub. No. US2002/0098477). The rejection is traversed on the grounds that the Patent Office has failed to establish a *prima facie* case of obviousness.

Claim 5 is dependent on Claim 1. Thus, Claim 5 recites a method for screening for an agent as set forth in Claim 1, wherein the reporter gene encodes a fluorescent protein.

As set forth in the section above discussing anticipation, *Glimcher* fails to teach or suggest the introduction of a plurality of candidate agents comprising a pool of expression vectors. Thus, *Glimcher* and *Kushner* taken together do not teach or suggest all of the elements of independent Claim 1. Accordingly, Claim 5 is not obvious in view these references.

Rejection of Claims 10 and 12-13 under 35 U.S.C. §103

Claims 10 and 12-13 stand rejected under 35 U.S.C. §103 as being obvious over Glimcher *et al.* (US Patent No. 5,958,67) or Kushner *et al.* (WO 99/11760), in view of Cen *et al.* (US Patent App. No. 2003/0170656). The rejection is traversed on the grounds that the Patent Office has failed to establish a *prima facie* case of obviousness.

Claims 10 and 12-13 ultimately depend from Claim 1. Accordingly, the Examiner has also failed to establish a prima facie case of obviousness in each of those Claims, as the Examiner has not shown that the cited references teach or suggest, alone or in combination, each and every claim limitation of Claim 1. Therefore, withdrawal of each of those rejections of Claims 10 and 12-13 is also respectfully requested.

Conclusion

Based on the foregoing, Applicants submit Claims 1-10, 12 and 13 are in condition for allowance. An early indication of the same is therefore respectfully requested. If any matters can be resolved by telephone, the Examiner is invited to call the undersigned attorney at the telephone number (415) 781-1989.

Respectfully submitted,

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Customer No. 32940

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